L6 ANSWER 13 OF 23 CAPLUS COPYRIGHT 2000 ACS
AN 1997:76308 CAPLUS
DN 126:140589
TI Mammalian germ cell mutagenicity of **ENU**, IPMS and MMS, chemicals selected for a transgenic mouse collaborative study
AU Shelby, Michael D.; R. Tindall, Kenneth
CS Reproductive Toxicology Group, NIEHS, P.O. Box 12233, Research Triangle Park, NC, 27709, USA
SO Mutat. Res. (1997), 388(2,3), 99-109
CODEN: MUREAV; ISSN: 0027-5107
PB Elsevier
DT Journal; **General Review**
LA English
AB A review and discussion with many refs. A collaborative study to systematically assess transgenic mouse mutation assays as screens for germ cell mutagens has been conducted. Three male mouse germ cell mutagens (**ENU**, iso-Pr methanesulfonate (IPMS) and MMS (Me methanesulfonate)) were selected for testing. This paper provides a brief review of the effects reported for those 3 chems. in the most commonly used non-transgenic germ cell mutagenicity assays, namely the dominant lethal, heritable translocation, and specific locus tests. Addnl., information on the DNA reactivity and the mol. nature of mutations induced by these

L6 ANSWER 7 OF 23 CAPLUS COPYRIGHT 2000 ACS
AN 1998:467394 CAPLUS
DN 129:198505
TI Large scale **ENU** screens in the mouse: genetics meets genomics
AU Hrabe de Angelis, Martin; Balling, Rudi
CS Institute of Mammalian Genetics, GSF Research Center for Environment and Health, Neuherberg, 85764, Germany
SO Mutat. Res. (1998), 400(1,2), 25-32
CODEN: MUREAV; ISSN: 0027-5107
PB Elsevier Science B.V.
DT Journal; **General Review**
LA English
AB A review with 51 refs. on the use of ethylnitrosourea (**ENU**) for chem. mutagenesis in the mouse. The worldwide effort to completely sequence the human and mouse genome will be accomplished within the next years. The focus of current activities within the framework of human genome research is mainly on the assembly of high resoln. genetic and phys. maps and genomic sequencing. Cloning of new genes is getting more easy using those maps. Nevertheless, it is necessary to work on a systematic anal. of gene function. Results obtained from these efforts will be of enormous value for future biol. and biomedical research. However, even the complete sequence will not in all cases reveal the mol. and cellular role of the different genes. Therefore, the next phase of the Human Genome Project will have at its core the functional anal. of genes. Those genes relevant for the diagnosis, prevention and therapy of human diseases are of particular interest. Looking at the history of life sciences, mutants have been the most important tool to obtain insight into the biol. function of genes. The mouse is the model of choice for the study of inherited diseases in man. In order to meet the requirements for functional human genome anal., we need a large no. of mouse mutants similar to the collection of mutants available for other model organisms such as flys and worms. To fully apply the power of genetics, multiple alleles of the same gene such as hypomorphs or hypermorphs are required. Efficient prodn. of mouse mutants showing specific phenotypes can be achieved by the use of **ENU**. **ENU** is the most powerful mutagen known and we currently see a renaissance of **ENU** mutagenesis. The application of **ENU** mutagenesis is reviewed and discussed in the context of a new era of functional genomics.

L6 ANSWER 6 OF 23 CAPLUS COPYRIGHT 2000 ACS
AN 1998:652091 CAPLUS
DN 130:21032
TI Mouse mutagenesis-systematic studies of mammalian gene function
AU Brown, Steve D. M.; Nolan, Patrick M.
CS MRC Mammalian Genetics Unit and Mouse Genome Centre, Harwell/Oxon, OX11 0RD, UK
SO Hum. Mol. Genet. (1998), 7(10, Rev. Issue), 1627-1633
CODEN: HMGEE5; ISSN: 0964-6906
PB Oxford University Press
DT Journal; **General Review**
LA English
AB A review with 45 refs. The mouse will play a role in mammalian gene function studies as we enter the post-genomics era. The challenge is to develop systematic, genome-wide mutagenesis approaches to the study fo gene function. The current mouse mutant resource has been an important source of human genetic disease models. However, despite an apparently large catalog of mouse mutations, we have access to mutations at only a small fraction of the likely total no. of mammalian genes-there is a phenotype gap that needs to be filled by the establishment of new mutagenesis programs. Two routes, genotype- and phenotype-driven, can be used for the recovery of novel mouse mutations. For the former, gene trap
embryonic stem cell libraries appear set to deliver a large no. of mutations around the mouse genome. The advantage of genotype-driven approaches is the ease of identification of the mutated locus; the disadvantage that a prior assumptions have to be made concerning the function and likely phenotype of the mutated gene. In contrast, phenotype-driven mutagenesis emphasizes the recover ov novel phenotypes. One phenotype-driven approach that will play an important role in expanding the mouse mutant resource employs the mutagen N-ethyl-N-nitrosourea (**ENU**). The phenotype-driven route makes no assumptions about the underlying genes involved, an **ENU** mutagenesis programs can be expected to play a significant role in uncovering novel pathways and genes; the disadvantage is that the identification of the mutant gene is still not trivial. Together, the complementary routes of genotype- and phenotype-driven mutagenesis will provide a much enlarged catalog of mouse mutations andphenotypes for future gene function studies.
RE.CNT 45
RE
(1) Albrecht, U; Cell 1997, V91, P1055 CAPLUS
(2) Antoch, M; Cell 1997, V89, P655 CAPLUS
(3) Ashburner, M; Curr Opin Genet Dev 1997, V7, P750 CAPLUS
(4) Bode, V; Genetics 1988, V118, P299 CAPLUS
(5) Bork, P; Nature Genet 1998, V18, P313 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 2 OF 23 CAPLUS COPYRIGHT 2000 ACS
AN 1999:673606 CAPLUS
DN 132:31315
TI Mouse **ENU** mutagenesis
AU Justice, Monica J.; Noveroske, Janice K.; Weber, John S.; Zheng, Binhai; Bradley, Allan
CS Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, TX, 77096, USA
SO Hum. Mol. Genet. (1999), 8(10), 1955-1963
CODEN: HMGEE5; ISSN: 0964-6906
PB Oxford University Press
DT Journal; **General Review**
LA English
AB A review with 67 refs. The progress of human genome sequencing is driving genetic approaches to define gene function. Strategies such as gene traps and chem. mutagenesis will soon generate a large mutant mouse resource. Point mutations induced by N-ethyl-N-nitrosourea (**ENU**) provide a unique mutant resource because they: (1) reflect the consequences of single gene change independent of position effects; (2) provide a fine-structure dissection of protein function; (3) display a range of mutant effects from complete or partial loss of function to exaggerated function; and (4) discover gene functions in an unbiased manner. Phenotype-driven **ENU** screens in the mouse are emphasizing relevance to human clin. disease by targeting cardiol., physiol., neurol., immunity, hematopoiesis and mammalian development. Such approaches are extremely powerful in understanding complex human diseases and traits: the base-pair changes may accurately model base changes found in human diseases, and subtle mutant alleles in a std. genetic background provide the ability to analyze the consequences of compd. genotypes. Ongoing mouse **ENU** mutagenesis expts. are generating a treasure trove of new mutations to allow an in-depth study of a single gene, a chromosomal region or a biol. system.
RE.

L24 ANSWER 5 OF 6 MEDLINE DUPLICATE 3
AN 1998149967 MEDLINE
DN 98149967
TI Random mutagenesis screen for dominant behavioral mutations in mice.
AU Nolan P M; Kapfhamer D; Bucan M
CS Center for Neurobiology and Behavior, University of Pennsylvania School of Medicine, Philadelphia 19104, USA.
NC HD 28410 (NICHD)
SO METHODS, (1997 Dec) 13 (4) 379-95. Ref: 95
Journal code: CPO. ISSN: 1046-2023.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199805
EW 19980503
AB Large-scale mutagenesis and screening for altered **phenotypes** have been used effectively in many (lower) model organisms to identify mutations in genes that control biological processes. In the mouse, the cost of maintaining the large **breeding** colonies necessary to screen for recessive mutations makes it important to consider alternate approaches such as region-specific saturation mutagenesis or screening for mutations with a dominant mode of inheritance. In this article, a pilot screen for (semi)dominant visible and behavioral mutations in the mouse induced by a potent chemical mutagen, N-ethyl-N-nitrosourea (**ENU**), is described. An efficient protocol for **ENU** mutagenesis and strain-specific differences in the effect of mutagen on the sterility period and long-term survival are reported. In addition to a description of the screen for abnormal circadian wheel running activity that was used previously, the suitability of a high-throughput screen of mutagenized progeny in the Porsolt swim test, used to test the efficacy of antidepressant agents, and in the prepulse inhibition of the acoustic startle response, used to detect anomalies in sensorimotor gating, is tested. By demonstrating strain specific differences and prescreening 100 G1 progeny of mutagenized males, the feasibility of using these behavioral assays for a large-scale screen is illustrated. In this review, details of a mutagenesis screen for behavioral abnormalities are described and issues important in the initial characterization of novel **ENU**-induced mutations are considered.